found at, for example, page 29, lines 24-28 of the specification. Support for the amendments to claim 38 and the newly added claims 40 and 41 can be found at, for example, page 27, lines 16-17 of the specification.

The Examiner has objected to the drawings in the present specification as being informal. Applicants respectfully submit that Formal Drawings will be submitted along with the payment of the Issue Fee, once the pending claims are allowed.

No new matter has been added. Any amendments to and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Objection of the Disclosure

The Examiner has objected to the specification because the ATCC accession number is not indicated.

Applicants respectfully submit that pursuant to *In re Lundak*, Applicants have the right to make a deposit of a plasmid containing a nucleotide sequence encoding the NIP2b, NIP2cL, and NIP2cS molecules of the present invention, prior to issuance of the application. *In re Lundak* 723 F2.d 1216, 227 USPQ 90 (Fed. Cir. 1985). Accordingly, Applicants reserve the right to amend the specification as originally filed to include the ATCC Deposit information for these molecules prior to issuance of the application.

Rejection of Claims 1-2, 4-5, 8-12 and 29-39 Under 35 U.S.C. § 101

The Examiner has rejected claims 1-2, 4-5, 8-12, and 29-39 under 35 U.S.C. § 101 because, according to the Examiner, "the claimed invention is not supported by either a specific and substantial utility or a well established utility." In particular, the Examiner is of the opinion that

> [a]ll function of the encoded proteins is by inference; no information is provided that the instant genes & constructs do indeed regulate apoptosis under any conditions. A starting material that can only be used to produce a final product

does not have a substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the proteins that are to be produced as final products resulting from processes involving the claimed cDNA have asserted or identified specific and substantial utilities. The research contemplated by Applicants to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of the protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the cDNA compounds such that another non-asserted utility would be well established for the compounds.

The Examiner further argues that "[a] sequence search by the examiner of SEQ ID NO:1, for example, showed that nucleotides 2585-3076 share an approximately 80% similarity to human sialoadhesin family 4 (SAF-1) cDNA, that nucleotides 2609-3076 also share an approximately 82% similarity to a nucleic acid encoding human aminopeptidase P (see attached sequence comparisons)" and that "[b]ecause the results of the examiner's search revealed a high degree of sequence similarity to genes encoding proteins unrelated to NIP2, further doubt is cast upon the utility and function of these disclosed sequences."

Applicants respectfully traverse the foregoing rejection for the following reasons. Applicants respectfully submit that a *well established utility* is immediately apparent from Applicants' specification and the knowledge in the art at the time of Applicants' invention. Specifically, Applicants have disclosed in the instant specification that the NIP molecules of the present invention play a role in apoptosis and that, therefore, these molecules provide novel diagnostic targets and therapeutic agents for disorders characterized by deregulated programmed cell death (see page 11, lines 16-33 of the specification). Moreover, it was well known in the art at the time of the present invention that NIP family members, *e.g.*, NIP2 and NIP3, induce apoptosis by, for example, interacting with Bcl-2 and suppressing its effects (see Chen G. *et al.* (1997) *J. Exp. Med.* 186(12):1975-1983 and Boyd J.M. *et al.* (1994) *Cell* 79:341-351, provided herewith as Appendices B and C, respectively). Applicants' specification further discloses that the NIP2 molecules of the present invention interact with the known adenovirus E1B 19 kDa

protein and the known Bcl-2 protein (see, for example, page 2, lines 15-18 of the specification). The Bcl-2 oncogene is known to enhance the survival of cells (*e.g.*, hematopoietic B and T cells) by blocking apoptosis (see Sentman *et al.* (1991) and Strasser *et al.* (1991), provided herewith as Appendices D and E, respectively). Thus, it is evident that based on Applicants' disclosure of the properties of the NIP2 molecules of the present invention and the knowledge of one skill in the art, a specific, substantial, and credible utility was immediately apparent for the present invention: *the use of the claimed invention to modulate apoptosis.*

Furthermore, as disclosed in Applicants' specification, the NIP molecules of the present invention may be used in tissue typing to identify individuals from minute biological samples and in forensic biology (a scientific field employing genetic typing of biological evidence found at a crime scene as a means for positively identifying, for example, a perpetrator of a crime) (see page 57, line 1, through page 58, line 30 of the specification). Thus, the NIP molecules of the present invention have various "real world" uses, such as in crime scene analyses and paternity determinations.

In addition, the fact that the Examiner has been able to find two sequences that are homologous at the nucleotide level to *small portions* of Applicants' nucleotide sequences (residues 2585-3076 and 2609-3076) should not cast doubt into Applicants' assertion that the disclosed polypeptides encoded by these nucleotide sequences are members of the NIP2 family of proteins. Applicants respectfully submit that residues 2585-3076 and 2609-3076 of SEQ ID NO:1 are *not even a part of the coding region* for the NIP2b cDNA. The coding region for this molecule is between nucleotide residues 370-1482 of SEQ ID NO:1 (see the Sequence Listing at page 78 of the specification). Thus, as is well known in the art, the Examiner's alignment results do not represent credible evidence that would support a function for the molecules of the present invention as the alignments have identified homologies to *a small portion of the non-coding region* of one of Applicants' nucleotide sequences.

Unlike the Examiner's alignments, Applicants' specification contains alignments of the *full amino acid sequences* of the NIP2b and NIP2cL polypeptides of the invention with the known BNIP-2 protein (Accession Number U15173). These alignments (Figures 10 and 12)

show a homology between these protein sequences that supports Applicants' assertion that the molecules of the present invention belong to the NIP2 family of proteins.

In view of the foregoing, it is evident that Applicants' invention has a specific, substantial, and credible utility that would have been readily apparent to one of skill in the art. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing section 101 rejection of claims 1-2, 4-5, 8-12 and 29-39.

Rejection of Claims 1-2, 4-5, 8-12, and 29-39 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1-2, 4-5, 8-12, and 29-39 under 35 U.S.C. §112, first paragraph because, according to the Examiner, "since the claimed invention is not supported by either a specific and substantial utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention."

Applicants respectfully traverse the foregoing rejection because, as indicated above, the claimed invention has a well established utility and, thus, one of skill in the art would know how to use the claimed invention. Moreover, Applicants' specification discloses *ample* guidance as to how one of skill in the art would use the claimed invention (see, for example, the screening assays, the diagnostic assays, the prognostic assays, and the methods of treatment, *e.g.*, therapeutic and prophylactic, taught by Applicants at page 47, line 28, through page 71, line 29 of the specification).

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing section 112, first paragraph rejection.

Rejection of Claim 8 Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claim 8 under 35 U.S.C. §112, second paragraph, as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that "[i]t is unclear whether the claim is directed to a nucleic acid comprising the instantly disclosed polynucleotide sequences and one encoding a heterologous protein (which may not be

contiguous) or whether the claimed nucleic acid encodes a fusion protein comprising the instantly disclosed nucleotide sequences joined to a heterologous sequence."

Applicants respectfully submit that the aforementioned rejection has been rendered moot in view of the amendments to the claims. Specifically, claim 8 has been amended to recite "[a]n isolated nucleic acid molecule comprising the nucleic acid molecule of any one of claims 1, 2, 5, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 40, or 41 ***operatively linked*** to a nucleotide sequence encoding a heterologous polypeptide, wherein said isolated nucleic acid molecule encodes a ***fusion polypeptide***." As indicated in the specification, "[w]ithin the fusion protein, the term 'operatively linked' is intended to indicate that the NIP2b, NIP2cL, and NIP2cS polypeptide and the non-NIP2b, NIP2cL, and NIP2cS polypeptide are fused in-frame to each other" (see page 29, lines 26-28 of the specification). Thus, the terms used in claim 8 are clear and definite in view of the teachings provided by Applicants in the specification.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this section 112, second paragraph rejection of claim 8.

Rejection of Claims 9, 11, 12, 38, and 39 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 9, 11, 12, 38, and 39 under 35 U.S.C. §102(b) as being anticipated by Boyd *et al.* (1994) *Cell,* 79:341-351. The Examiner relies on Boyd *et al.* for teaching a "cDNA encoding Nip2 (Genbank accession # U15173), plasmids containing the construct and recombinantly produced protein." The Examiner is of the opinion that Boyd *et al.* "is deemed anticipatory for the claimed subject matter because nucleotides 908-976 of Nip2 encode amino acids 257-279 of SEQ ID NO:2 (see attached sequence comparison) and thus comprises a nucleotide which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2."

Applicants respectfully submit that the aforementioned rejection has been rendered moot in view of the amendments to the claims. Specifically, amended claim 38 and claims depending therefrom, are directed to isolated nucleic acid molecules encoding polypeptide fragments of at

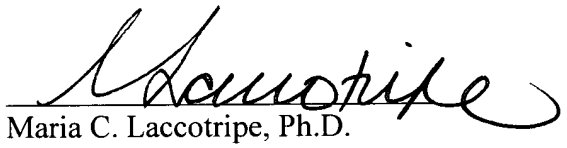
least ***25 contiguous amino acid residues*** of the amino acid sequence of SEQ ID NO:2, 5, or 8. As indicated by the Examiner, the nucleic acid molecule disclosed by Boyd *et al.* encodes amino acids 257-279 of SEQ ID NO:2, *i.e.*, a fragment of ***23 amino acid residues***. Thus, Boyd *et al.* do not teach each and every element of amended claim 38 and claims depending therefrom.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this section 102(b) rejection of claims 9, 11, 12, 38, and 39.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If a telephone conversation with Applicants' Agent would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



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Limited Recognition Under 37 C.F.R§10.9(b)

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